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(FILE 'HOME' ENTERED AT 13:57:03 ON 23 JAN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 13:57:18 ON 23 JAN 2003

L1 13198 S (INFUSION OR OSMOTIC)(W)PUMP
L2 98582 S GENE(3A)(DELIVER? OR THERAPY)
L3 6 S L1(7A)L2
L4 6 DUP REM L3 (0 DUPLICATES REMOVED)

=> d 1-6 au ti so ab l4

L4 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU Roguin, A. (1); Nitecki, S. (1); Rubinstein, I.; Resnik, M. D.; Levy, N. S.; Abassi, Z.; Lache, O.; Beyar, R. (1); Hoffman, A. (1); Levy, A. P.
TI A novel method for gene therapy delivery: Continuous perimuscular infusion of naked-DNA encoding VEGF.
SO European Heart Journal, (September, 2001) Vol. 22, No. Abstract Supplement, pp. 625. print.
Meeting Info.: XXIII Congress of the European Society of Cardiology together with the 36th Annual General Meeting of the Association for European Paediatric Cardiology Stockholm, Sweden September 01-05, 2001
ISSN: 0195-668X.

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
IN Kundig, Thomas M.; Simard, John J. L.
TI A method of inducing a CTL response
SO PCT Int. Appl., 199 pp.
CODEN: PIXXD2
AB A method of inducing a cytotoxic T-lymphocyte (CTL) response to an antigen is disclosed. The method involves delivering the antigen to the lymphatic system of an animal regularly over a sustained period of time using, e.g., an osmotic pump. The method is advantageous over prior art methods for inducing a CTL response in that it does not require repetitive immunizations or the use of adjuvants. The method of the present invention can be used for the induction of CTLs in tumor or infectious disease immunotherapy.

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
AU Kramer, Kenneth L.; Giffin, Bruce F.; Fox, James W.; Drake, Richard L.
TI Insulin replacement therapy in diabetic rats using an osmotic pump normalizes expression of enzymes key to hepatic carbohydrate metabolism
SO Archives of Biochemistry and Biophysics (1999), 368(2), 291-297
CODEN: ABBIA4; ISSN: 0003-9861
AB Intensively treating type I diabetics with continuous s.c. insulin infusions or multiple daily insulin injections to normalize mean blood glucose concns. significantly reduces the onset of secondary diabetic complications when compared to conventionally treated diabetics. The authors' studies focused on characterizing hepatic enzyme expression in intensively and conventionally treated diabetic rats. Alloxan-induced diabetic rats were conventionally treated with insulin injected twice daily or intensively treated with similar daily dosages of insulin administered via a surgically implanted osmotic pump. The authors' results demonstrate a significant difference in hepatic enzyme expression when these treatment regimes are compared. In conventionally treated diabetic rats, phosphoenolpyruvate carboxykinase (PEPCK) protein and mRNA levels remained slightly elevated when compared to normal animals, glycogen phosphorylase (GP) protein levels were still slightly decreased, and glycogen synthase (GS) protein and mRNA levels remained at the elevated levels obsd. in untreated diabetics. In contrast, the protein and mRNA levels of all three enzymes were normalized in the insulin pump-treated animals. These results suggest that intensive insulin

therapy improves glycemia directly by normalizing hepatic gene expression while conventional insulin therapy normalizes plasma glucose concns. indirectly. (c) 1999 Academic Press.

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AU Alino, S. F.; Crespo, J.; Tarrason, G.; Blaya, C.; Adan, J.; Escrig, E.; Benet, M.; Crespo, A.; Piulats, J.
TI Oligonucleotide-entrapped immunoliposome delivered by mini-osmotic pump improves the survival of SCID mice bearing human leukemia
SO Tumor Targeting (1999), 4(1), 20-28
CODEN: TUTAF9; ISSN: 1351-8488
AB A study was made of the efficacy of CD45-targeted immunoliposomes entrapping c-myb antisense phosphorothioate oligonucleotides to increase survival in a scid mouse model of human leukemia. The encapsulation efficiency of oligonucleotides in backbone liposomes was optimized using a dehydration-rehydration procedure. Pharmacokinetic parameters indicate that the t1/2 of free oligonucleotide (0.14 .+-. 0.02 h) was increased 63-fold when the oligonucleotide was encapsulated in small liposomes, whereas clearance decreased 50-fold accordingly. Multivalent liposomes for targeting were prepd. by covalently coupled streptavidin on the liposome surface. The ability of streptavidin-liposomes to bind biotinylated antibodies was confirmed using biotin-peroxidase as tracer and size exclusion chromatog. as it allows differentiation of the proportion of enzymic activity in the liposome fraction vs. the free enzyme. The in vivo efficacy of CD45-targeted liposomes was evaluated on scid mice transplanted with K562 human leukemia cells. Three weeks after transplant, mice were treated with HEPES (N-[2-Hydroxyethyl] piperazine-N'-[2-ethanesulfonic acid]), free antisense oligonucleotide or liposome encapsulating sense or antisense oligonucleotides. In order to improve the pharmacokinetic properties of free and encapsulated oligonucleotides, administration was performed by continuous infusion employing mini-osmotic pumps. We obsd. that CD45-targeted liposomes entrapping antisense oligonucleotides greatly increased survival, which was > 60% six months after tumor transplant. However, free antisense or encapsulated sense oligonucleotide in CD45-targeted liposome did little to increase survival with respect to the animals treated with HEPES. These results suggest that targeted immunoliposomes can contribute to the success of antisense therapeutic strategies in leukemia.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
IN Lalwani, Anil; Schindler, Robert A.
TI Transformation and gene therapy of cells of the inner ear
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
AB Compns. and methods are disclosed for transformation of cells of the inner ear and treatment of conditions of the inner ear using such methods. More specifically, cells of an inner ear of a subject are genetically altered to operatively incorporate a nucleotide sequence which expresses a gene product of interest (e.g., a therapeutic gene product). Preferably, the inner ear cell into which the DNA of interest is introduced and expressed is a cell of the cochlea, more preferably a cell of the spiral ligament, spiral limbus, stria vascularis, organ of Corti, spiral ganglion, and/or Reissner's membrane, and/or an auditory hair cell. The DNA of interest, preferably present within an adeno-assocd. viral vector, is introduced through a cannula inserted in the round or oval window and in communication with the perilymph or endolymph. Preferably, introduction of the DNA of interest is accomplished using an osmotic minipump.

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
AU Zhu, J.; Zhang, L.; Hanisch, U. K.; Felgner, P. L.; Reszka, R.
TI A continuous intracerebral gene delivery system for in vivo liposome-mediated gene therapy
SO Gene Therapy (1996), 3(6), 472-476
CODEN: GETHEC; ISSN: 0969-7128

AB Using a minipump combined with stereotaxic techniques allows continuous delivery of therapeutic genetic materials into the brain. We investigated the therapeutic efficacy of liposome-mediated HSVtk gene transfer of exptl. brain F98 glioma followed by treatment with ganciclovir. A single injection of DNA-liposome complexes showed a therapeutically significant decrease in the tumor vol. Continuous intracerebral delivery of DNA-liposome complexes using an osmotic minipump led to complete tumor regression in 36.4% of the treated animals. The safety and toxicity of this gene delivery system were also assessed. No organ pathol. was obsd. in the exptl. animals. The continuous gene delivery system could be a useful means of achieving higher doses with less toxicity and without the need for frequent injections.

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L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1999:64705 CAPLUS
DN 130:138281
TI A method of inducing a CTL response
IN Kundig, Thomas M.; Simard, John J. L.
PA CTL Immunotherapies Corporation, Can.
SO PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902183	A2	19990121	WO 1998-US14289	19980710
	WO 9902183	A3	19990514		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9885689	A1	19990208	AU 1998-85689	19980710
	AU 739189	B2	20011004		
	EP 1003548	A1	20000531	EP 1998-936827	19980710
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001509490	T2	20010724	JP 2000-501773	19980710
	US 2002007173	A1	20020117	US 2001-776232	20010202
PRAI	CA 1997-2209815	A	19970710		
	US 1997-988320	A2	19971210		
	WO 1998-US14289	W	19980710		
	US 1999-380534	A2	19990901		

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1998:55483 CAPLUS
DN 128:97727
TI Transformation and gene therapy of cells of the inner ear
IN Lalwani, Anil; Schindler, Robert A.
PA Regents of the University of California, USA; Lalwani, Anil; Schindler, Robert A.
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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PI   WO 9800014         A1   19980108       WO 1997-US11602  19970627
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            LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
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            GN, ML, MR, NE, SN, TD, TG
     AU 9735915         A1   19980121       AU 1997-35915    19970627
PRAI US 1996-674231          19960628
     WO 1997-US11602         19970627


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